

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C. 20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing: 30 March 2000 (30.03.00)	
International application No.: PCT/EP99/07088	Applicant's or agent's file reference: 51656AWOM1 27-P
International filing date: 16 September 1999 (16.09.99)	Priority date: 18 September 1998 (18.09.98)
Applicant: FUJI PHOTO FILM CO., LTD. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International preliminary Examining Authority on:

22 February 2000 (22.02.00)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No.: (41-22) 740.14.35	Authorized officer:  J. Zahra Telephone No.: (41-22) 338.83.38
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## PATENT COOPERATION TREATY

PCT

REC'D 11 JAN 2001

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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

09787.394

Applicant's or agent's file reference 51656AWOM1XX27-P		<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP99/07088	International filing date (day/month/year) 16/09/1999	Priority date (day/month/year) 18/09/1998	<b>RECEIVED</b> MAR 14 2003 TECH CENTER 1600/2900
International Patent Classification (IPC) or national classification and IPC A61K49/00			
Applicant SCHERING AKTIENGESELLSCHAFT et al.			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 5 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 22/02/2000	Date of completion of this report 09.01.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4455	Authorized officer  Engl, B 

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP99/07088

**I. Basis of the report**

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:

**Description, pages:**

1-85 as originally filed

**Claims, No.:**

1-28 as originally filed

**Drawings, sheets:**

1/8-8/8 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☐ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP99/07088

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes: Claims
	No: Claims 1-4,7,15,24
Inventive step (IS)	Yes: Claims
	No: Claims 1-28
Industrial applicability (IA)	Yes: Claims 1-28
	No: Claims

**2. Citations and explanations  
see separate sheet**

**VI. Certain documents cited**

**1. Certain published documents (Rule 70.10)**

and / or

**2. Non-written disclosures (Rule 70.9)**

**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/EP99/07088

**Concerning Section V:**

The following documents are cited from the International Search Report:

- D1: WO-A-98/22146
- D2: WO-A-97/13810
- D3: WO-A-97/40104
- D4: WO-A-97/13490
- D5: WO-A-96/17628
- D6: EP-A-0 580 145
- D7: EP-A-0 591 820
- D8: PROCEEDINGS OF THE SPIE, vol. 2927, page 199-208
- D9: PROCEEDINGS OF THE SPIE, vol. 3196, page 98-102
- D10: PROCEEDINGS OF THE SPIE, vol. 2927, page 192-198

D1 describes compounds whose general formula overlaps with that found in present claim 1 for use in near infrared diagnosis of neurodegenerative diseases. D2, D3, D6 and D7 disclose (fluorescent) cyanine dyes containing several sulphonic acid groups for enhancing hydrophilicity and hence water-solubility. D4 and D5 describe cyanine dyes as contrast agents for near infrared diagnosis, D5, pages 23 and 24, D8, D9 and D10 point to the advantages of enhanced hydrophilicity in compounds which are intended to be used in near infrared imaging.

The disclosure of D1 is considered to fall within present claims 1 to 4, 7, 15 and 24. Novelty (Article 33 (2) PCT) cannot therefore be acknowledged.

Cyanine type dyes having enhanced hydrophilicity (water-solubility) and improved fluorescent properties due to a higher sulphonic acid group content are known from D2, D3, D6 and D7. The fact that enhanced hydrophilicity is desirable in compounds intended for diagnostic use is clear from D5, D8, D9 and D10. It was therefore obvious for one skilled in the art to modify cyanine dyes by attaching further sulphonic acid groups. Therefore, an inventive step (Article 33 (3) PCT) cannot be acknowledged for that subject-matter which is possibly novel

**Concerning Section VI:**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/EP99/07088

The document WO-A-98/47538 claims a priority date which is before, but was published after the present one. Priorities have not been checked, however, the said document might become relevant for the assessment of novelty and inventive step.

**Concerning Section VIII:**

If the proviso found in claim 1 (provided that when  $r$  is 2, .. different) is intended to exclude prior art that has not been cited so far, the latter could become relevant for assessing novelty and/or inventive step. Therefore, the reason for the said proviso should be communicated (Rule 5.1 (ii) PCT).

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 99/07088

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 A61K49/00

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 98 47538 A (WRASIDLO WOLFGANG ; LICHAKAI (DE); RIEFKE BJOERN (DE); DIAGNOSTIKF) 29 October 1998 (1998-10-29) page 13, line 29 -page 14, line 14 figures 3,4	1-4, 7, 24
X	WO 98 22146 A (LICHAKAI ; RIEFKE BJOERN (DE); DYRKSTHOMAS (DE); TURNER JONATHAN) 28 May 1998 (1998-05-28) page 6, line 19 -page 11, line 6; claims 11-13; examples 1-3	1-4, 7, 15, 24
Y	WO 97 13810 A (SORIN BIOMEDICA CARDIO SPA ; DELLA CIANA LEOPOLDO (IT); GRIGNANI AN) 17 April 1997 (1997-04-17) page 6, line 25 -page 9, line 15 page 10, line 29-35	1-28

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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

2 February 2000

Date of mailing of the international search report

11/02/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Engl, B

# INTERNATIONAL SEARCH REPORT

Int'l Application No

PCT/EP 99/07088

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 97 40104 A (BRIGGS MARK SAMUEL JONATHAN ;HAMILTON ALAN LEWIS (GB); WEST RICHAR) 30 October 1997 (1997-10-30) page 7, line 2-9; examples 2A,2E,6A,6B ---	1-28
Y	WO 97 13490 A (LICHIA KAI ;RIEFKE BJOERN (DE); HELDMANN DIETER (DE); DIAGNOSTIKFOR) 17 April 1997 (1997-04-17) cited in the application the whole document ---	1-28
Y	WO 96 17628 A (DIAGNOSTIKFORSCHUNG INST ;LICHIA KAI (DE); RIEFKE BJOERN (DE); SEMM) 13 June 1996 (1996-06-13) cited in the application the whole document ---	1-28
Y	EP 0 580 145 A (FUJI PHOTO FILM CO LTD) 26 January 1994 (1994-01-26) cited in the application page 3, line 11 -page 17, line 40 ---	1-28
Y	EP 0 591 820 A (DU PONT) 13 April 1994 (1994-04-13) cited in the application the whole document ---	1-28
Y	RIEFKE ET AL: "In vivo characterization of cyanine dyes as contrast agents for near-infrared imaging" PROCEEDINGS OF THE SPIE,US,SPIE, BELLINGHAM, VA, vol. 2927, page 199-208 XP002037276 the whole document ---	1-28
Y	LICHIA ET AL: "Synthesis and characterization of cyanine dye - poly(ethylene glycol) conjugates as contrast agents for in vivo fluorescence imaging" PROCEEDINGS OF THE SPIE,US,SPIE, BELLINGHAM, VA, vol. 3196, page 98-102 XP002079471 the whole document ---	1-28
Y	LICHIA ET AL: "Synthesis and characterization of cyanine dyes as contrast agents for near-infrared imaging" PROCEEDINGS OF THE SPIE,US,SPIE, BELLINGHAM, VA, vol. 2927, page 192-198 XP002079648 the whole document -----	1-28



# INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

PCT/EP 99/07088

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9847538 A	29-10-1998	DE 19717904 A AU 7905798 A NO 995181 A	29-10-1998 13-11-1998 22-10-1999
WO 9822146 A	28-05-1998	DE 19649971 A AU 7298598 A EP 0942756 A	28-05-1998 10-06-1998 22-09-1999
WO 9713810 A	17-04-1997	IT MI952049 A AU 706668 B AU 7288296 A CA 2234450 A EP 0876428 A	09-04-1997 17-06-1999 30-04-1997 17-04-1997 11-11-1998
WO 9740104 A	30-10-1997	EP 0898596 A	03-03-1999
WO 9713490 A	17-04-1997	DE 19539409 A AU 711266 B AU 1589297 A CA 2233995 A CN 1199341 A EP 0854732 A HU 9900458 A JP 11504656 T NO 981586 A	17-04-1997 07-10-1999 30-04-1997 17-04-1997 18-11-1998 29-07-1998 28-06-1999 27-04-1999 07-04-1998
WO 9617628 A	13-06-1996	DE 4445065 A AU 709152 B AU 3740995 A CA 2205906 A CN 1174511 A EP 0796111 A HU 77378 A JP 10510250 T NO 972509 A NZ 294568 A ZA 9509707 A	13-06-1996 19-08-1999 26-06-1996 13-06-1996 25-02-1998 24-09-1997 28-04-1998 06-10-1998 02-06-1997 30-08-1999 29-05-1996
EP 0580145 A	26-01-1994	JP 2955803 B JP 6043583 A US 5445930 A US 5738982 A	04-10-1999 18-02-1994 29-08-1995 14-04-1998
EP 0591820 A	13-04-1994	JP 2725981 B JP 6202281 A US 5397690 A	11-03-1998 22-07-1994 14-03-1995

# PATENT COOPERATION TREATY

# PCT

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REC'D 11 JAN 2001

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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>51656AWOM1XX27-P</b>	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. <b>PCT/EP99/07088</b>	International filing date (day/month/year) <b>16/09/1999</b>	Priority date (day/month/year) <b>18/09/1998</b>
International Patent Classification (IPC) or national classification and IPC <b>A61K49/00</b>		
Applicant <b>SCHERING AKTIENGESELLSCHAFT et al.</b>		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of    sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li>I    <input checked="" type="checkbox"/> Basis of the report</li> <li>II   <input type="checkbox"/> Priority</li> <li>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li> <li>IV <input type="checkbox"/> Lack of unity of invention</li> <li>V   <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li>VI <input checked="" type="checkbox"/> Certain documents cited</li> <li>VII <input type="checkbox"/> Certain defects in the international application</li> <li>VIII <input checked="" type="checkbox"/> Certain observations on the international application</li> </ul>		
Date of submission of the demand  <b>22/02/2000</b>	Date of completion of this report  <b>09.01.2001</b>	
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  <b>Engl, B</b>  Telephone No. +49 89 2399 8283	



# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP99/07088

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

### 1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	1-4,7,15,24
Inventive step (IS)	Yes: Claims	
	No: Claims	1-28
Industrial applicability (IA)	Yes: Claims	1-28
	No: Claims	

2. Citations and explanations  
**see separate sheet**

## VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

**see separate sheet**

## VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
**see separate sheet**

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP99/07088

## I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).):*

### Description, pages:

1-85 as originally filed

### Claims, No.:

1-28 as originally filed

### Drawings, sheets:

1/8-8/8 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>51656AWOM1 27-P</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/EP 99/ 07088</b>	International filing date (day/month/year) <b>16/09/1999</b>	(Earliest) Priority Date (day/month/year) <b>18/09/1998</b>
Applicant <b>SCHERING AKTIENGESELLSCHAFT et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

**NEAR INFRARED FLUORESCENT CONTRAST AGENT AND FLUORESCENCE IMAGING**

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/EP99/07088

**Concerning Section V:**

The following documents are cited from the International Search Report:

- D1: WO-A-98/22146
- D2: WO-A-97/13810
- D3: WO-A-97/40104
- D4: WO-A-97/13490
- D5: WO-A-96/17628
- D6: EP-A-0 580 145
- D7: EP-A-0 591 820
- D8: PROCEEDINGS OF THE SPIE, vol. 2927, page 199-208
- D9: PROCEEDINGS OF THE SPIE, vol. 3196, page 98-102
- D10: PROCEEDINGS OF THE SPIE, vol. 2927, page 192-198

D1 describes compounds whose general formula overlaps with that found in present claim 1 for use in near infrared diagnosis of neurodegenerative diseases. D2, D3, D6 and D7 disclose (fluorescent) cyanine dyes containing several sulphonic acid groups for enhancing hydrophilicity and hence water-solubility. D4 and D5 describe cyanine dyes as contrast agents for near infrared diagnosis, D5, pages 23 and 24, D8, D9 and D10 point to the advantages of enhanced hydrophilicity in compounds which are intended to be used in near infrared imaging.

The disclosure of D1 is considered to fall within present claims 1 to 4, 7, 15 and 24. Novelty (Article 33 (2) PCT) cannot therefore be acknowledged.

Cyanine type dyes having enhanced hydrophilicity (water-solubility) and improved fluorescent properties due to a higher sulphonic acid group content are known from D2, D3, D6 and D7. The fact that enhanced hydrophilicity is desirable in compounds intended for diagnostic use is clear from D5, D8, D9 and D10. It was therefore obvious for one skilled in the art to modify cyanine dyes by attaching further sulphonic acid groups. Therefore, an inventive step (Article 33 (3) PCT) cannot be acknowledged for that subject-matter which is possibly novel

**Concerning Section VI:**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

---

International application No. PCT/EP99/07088

The document WO-A-98/47538 claims a priority date which is before, but was published after the present one. Priorities have not been checked, however, the said document might become relevant for the assessment of novelty and inventive step.

**Concerning Section VIII:**

If the proviso found in claim 1 (provided that when  $r$  is 2, .. different) is intended to exclude prior art that has not been cited so far, the latter could become relevant for assessing novelty and/or inventive step. Therefore, the reason for the said proviso should be communicated (Rule 5.1 (ii) PCT).